

**This Page Is Inserted by IFW Operations
and is not a part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- **BLACK BORDERS**
- **TEXT CUT OFF AT TOP, BOTTOM OR SIDES**
- **FADED TEXT**
- **ILLEGIBLE TEXT**
- **SKEWED/SLANTED IMAGES**
- **COLORED PHOTOS**
- **BLACK OR VERY BLACK AND WHITE DARK PHOTOS**
- **GRAY SCALE DOCUMENTS**

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

JP 04-182,423

Translated from Japanese by the Ralph McElroy Co., Custom Division
P.O. Box 4828, Austin, Texas 78765 USA

1
Code: 282-59319

JAPANESE PATENT OFFICE
PATENT JOURNAL
KOKAI PATENT NO. HEI 4[1992]-182423

Int. Cl. ⁵ :	A 61 K 7/50 31/16 31/195 //A 61 K 35/78 C 11 D 3/48
Sequence Nos. for Office Use:	7252-4C 8413-4C 8413-4C 7180-4C 7614-4H
Application No.:	Hei 2[1990]-311040
Application Date:	November 16, 1990
Publication Date:	June 30, 1992
No. of Claims:	1 (Total of 7 pages)
Examination Request:	Not requested

COMPOSITION FOR CLEANING AND WIPING

Inventors:

Eriko Kasahara
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Kenji Kitamura
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Yasukazu Nakayama
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Naoe Akiyama
Shiseido Co., Ltd.
Research Center,
1050 Shinbane-cho,
Kohoku-ku, Yokohama-shi,
Kanagawa-ken

Applicant:

Shiseido Co., Ltd.
7-5-5 Ginza, Chuo-ku,
Tokyo

[There are no amendments to this patent.]

inflammation, abrasion, etc., at the periphery of the anus and thus, it is not desirable.

Furthermore, in the case of infants and elderly persons with diapers, paper material such as toilet paper and cleaning cottons are generally used to wipe excreta. The excreta comes into contact with the skin for a relatively long period of time in the case of infants and elderly persons with diapers, thus, the excreta itself causes irritation, and the anus and its periphery frequently have symptoms of inflammation, abrasion, itching, etc.

As a means to solve this problem, there are known cleaners in the form of aerosols, wet tissue paper, oil, etc., and they have good cleaning effects but some cause irritation or inflammation becoming undesirable with respect to safety.

Problems to be solved by the invention

The inventors of this invention studied diligently under the circumstances described above, and as a result, they found it possible to prepare a composition having excellent cleaning power and remarkably reduced skin irritation by compounding those cleaners in the form of aerosols, wet tissue, oil, etc., with compounds having a protease inhibitory action, and they arrived at this invention.

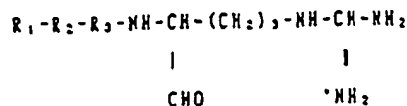
Means to solve the problems

Specifically, this invention is a composition for cleaning and wiping characterized by containing one or more compounds having protease inhibitory action.

The configuration of this invention is explained as follows.

(2) Compounds of microorganism origin

There are preferably antipain, plasminostreptin, compounds generically called leupeptin represented by the following general formula, etc.



$R_1 = CH_3CO, CH_3CH_2CO$

$R_2 = L\text{-Leu}, L\text{-Ile}, L\text{-Val}$

$R_3 = L\text{-Leu}, L\text{-Ile}, L\text{-Val}$

(Leu: leucine, Ile: isoleucine, Val: valine)

(3) Benzamidine and its derivatives

There are preferably benzamidine, p-aminobenzamidine, m-aminobenzamidine, phenylguanidine, (2R,4R)-4-methyl-1-[N²-(3-methyl-1,2,3,4-tetrahydro-8-quinolinesulfonyl)-L-alginyll]-2-piperidinecarboxylic acid monohydrate, dansylarginine N-(3-ethyl-1,5-pentanyl)amide, etc.

(4) Acetamide and its derivatives

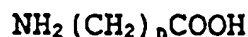
There are preferably acetamide, 2-phenylacetamide, cyclohexylchioxamide [transliteration], etc.

(5) Guanidine and its derivatives

There are preferably phenylguanidine, cyclohexylguanidine, etc.

(6) ω -Amino acid

There are preferably tranexamic acid, p-aminomethylbenzoic acid, 4-aminomethylbicyclo[2.2.2.]octane-1-carboxylic acid, 5-[trans-4-(aminomethyl)cyclohexyl]tetrazole, 3-[trans-4-(aminomethyl)cyclohexyl-2-oxopropionate, trans-4-(aminomethyl)cyclohexylglyoxal monohydrate, trans-4-(aminomethyl)cyclohexane hydroxamic acid, etc., as well as compounds of the following general formula with $n = 1-8$.



It is not necessarily limited to these compounds in this invention. Among those ω -amino acids, tranexamic acid and p-aminomethylbenzoic acid showed especially excellent effects.

(7) Fluorophosphoric acid and its derivatives

There are preferably diisopropylfluorophosphoric acid, etc.

(8) Fluorosulfonic acid and its derivatives

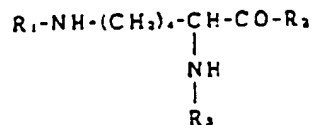
There are preferably phenylmethane sulfonylfluoride, (p-amidinophenyl)methane sulfonylfluoride, etc.

(9) Guanidinobenzoic acid and its derivatives

There are preferably p-nitrophenyl-p'-guanidinobenzoic acid, 3',6'-bis[4-guanidinobenzoyloxy]-5-(N'-4-carboxyphenyl)-thioureidospiro[isobenzofuran-1(3H),9'-(9H) xanthane]-3-one, etc.

(10) Lysine and its derivatives

There are preferably compounds represented by the following general formula:



$R_1 = H, Phe-Ala, Ala-Phe$

$R_2 = OH, CH_2Cl$

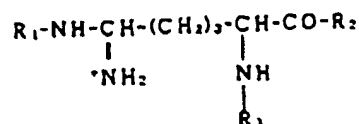
$R_3 = H, SO_2-C_6H_4-CH_3$

(Phe: phenylalanine, Ala: alanine)

It is not necessarily limited to these compounds in this invention, and among lysine and its derivatives, the effects of the compound with $R_2 = CH_2Cl$ are especially excellent.

(11) Arginine and its derivatives

There are preferably compounds represented by the following general formula:



$R_1 = H, D-Phe-Pro, Glu-Gly,$
 $Ile-Glu-Gly, Pro-Phe,$
 $Ala-Phe$

$R_2 = OH, CH_2Cl$

$R_3 = H, SO_2-\text{C}_6\text{H}_5-CH_3$

(Phe: phenylalanine, Pro: proline, Glu: glutamic acid, Gly: glycine, Ile: isoleucine, Ala: alanine)

It is not necessarily limited to these compounds in this invention, and among arginine and its derivatives, the effects of the compound with $R_2 = CH_2Cl$ are especially excellent.

In this invention, these proteinase inhibitors may be used alone or as a mixture of two or more kinds.

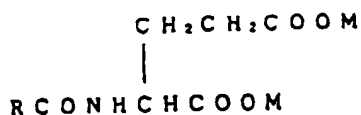
The amount of such protease inhibitors to be compounded in the cleaning and wiping composition of this invention is desirably 0.0001-20 wt%, preferably 0.001-5 wt% of the whole amount of the composition. If it is less than 0.0001 wt%, the effects of this invention are not sufficient, and if it is over 20 wt%, it is undesirable with respect to formulation process, and it is disadvantageous with respect to cost.

iii) N-Acylsarcosinate-type anionic surfactants represented by the following general formula:



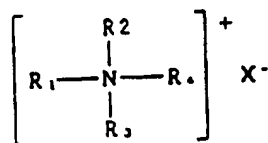
(In the formula, R is an alkyl or alkenyl group having 8-18 carbon atoms, M is an alkali metal, organic amine or basic amino acid alone or a mixture of two or more kinds.)

iv) Anionic surfactants having a -COO^- group such as condensation products of higher fatty acids such as N-acylglutamate represented by the following general formula with amino acids:



(In the formula, R is an alkyl or alkenyl group having 8-18 carbon atoms, M is an alkali metal, organic amine or basic amino acid alone or a mixture of two or more kinds.)

As cationic surfactants, there are monoalkyl quaternary ammonium salts represented by the following general formula:



(where R_1 is an alkyl or alkenyl group having 12-22 carbon atoms, R_2 , R_3 and R_4 are methyl or ethyl groups, X is a halogen atom or methylsulfate residual group), fatty acid amine salts, aromatic quaternary ammonium salts, pyridinium salts, imidazolinium salts, etc.

As nonionic surfactants, there are glycerine fatty acid esters, sorbitan fatty acid esters, sorbitol fatty acid esters, sucrose fatty acid esters, polyoxyethylenes (abbreviated to POE, below) sorbitan fatty acid esters, polyoxyethylene glycol fatty acid esters, POE alkyl ethers, POE alkyl phenyl ethers, POE-hardened castor oil derivatives, mannitol hydroxyfatty acid ethers, alkyl glucoside fatty acid ethers, etc.

As ampholytic surfactants, there are carboxybetaines such as N,N-dimethyl-lauryl-N-carboxymethylammonium betaine, N,N-dimethyl-N-oleyl-N-carboxymethylammonium betaine, lauryldimethylaminoacetic acid, etc.; imidazoline derivatives such as 2-lauryl-N-carboxyethyl-N-hydroxyethylimidazolium betaine, 2-lauryl-N-carboxymethyl-N-hydroxyethylimidazolium betaine, sodium 2-undecyl-N,N,N-(hydroxyethylcarboxymethyl)-2-imidazoline, 2-cocoyl-2-imidazoliumhydroxide-1-carboxyethyloxy-2-sodium, etc.; aminocarboxylates such as sodium N-coconut alkyl- β -aminopropionate, sodium N-coconut alkyl- β -iminodipropionate, etc.; sulfobetaine; aminobetaine; etc.

As semipolar surfactants, there are lauryldimethylamine oxide, stearyldimethylamine oxide, bis-(2-hydroxyethyl)laurylamine oxide, etc.

As a propellant, any propellant used for conventional aerosol products is usable. Specifically, there are fluorocarbons such as Flon 11 (registered trademark), Flon 12 (registered trademark), Flon 21 (registered trademark), Flon 113 (registered

ether, polyoxyalkylene decaglyceryl ether, polyoxyalkylene pentaerythritol ether, sorbitol, maltitol, lactose, D-mannitol, etc.

In addition, sterilizers such as cetylpyridinium chloride, benzethonium chloride, dequalinium chloride, benzalkonium chloride, chlorhexidine gluconate, carbanilide, phenol, halogenated salicylanilide, etc.; moisturizers, for example, bases such as sodium hydroxide, ammonia, etc.; lower alcohols such as ethanol, etc.; mucopolysaccharides; pyrrolidone carboxylate, etc., are also usable.

The formulation of the cleaning and wiping composition of this invention may be any of those formulation suitable for accomplishing the objective as a cleaning and wiping agent, and for example, there are liquids (lotion, emulsion), creams, aerosols, wet tissues, sprays, etc.

Effect of the invention

The composition for cleaning and wiping of this invention has excellent effects preventing and improving rough skin; at the same time, it is highly safe and shows excellent cleaning and wiping power in the case of practical applications for cleaning and wiping.

Application examples

This invention is explained specifically in detail by using application examples as follows, but this invention is not necessarily limited to these examples.

Before explaining these application examples, those testing and evaluation methods carried out to evaluate the low irritation (prevention and improvement of rough skin formation) of the protease inhibitors of this invention are explained first as follows.

Practical use test

The test subjects were 60 infants of relatively tender skin liable to have "diaper rash" separated into 6 groups of 10 babies each. Diapers were used, and the genitalia, anus and their peripheries were cleaned with the cleaning and wiping compositions shown in Table I. Those application examples were used in 5 groups, and the Comparative Example 1 was used in the remaining one group. After carrying out a 4-week application test, the state and condition of the skin after 4 weeks were examined by naked eye examination, and the standards shown in Table II were used for evaluation. Incidentally, the formulation in each example was an aerosol formulation prepared using conventional procedures.

Table II. Effects improving diaper rash

① 評価	② 判断基準
著効 ③	おむつかぶれが消失したもの
有効 ④	おむつかぶれが非常に改善したもの
やや有効 ⑤	おむつかぶれがやや改善したもの
無効 ⑥	おむつかぶれに変化を認めないもの
悪化 ⑦	おむつかぶれが悪化したもの

- Key: 1 Evaluation
 2 Evaluation standards
 3 Markedly effective: disappearance of diaper rash
 4 Effective: significantly improved diaper rash
 5 Slightly effective: slightly improved diaper rash
 6 Ineffective: no change in diaper rash
 7 Worsening: worsening of diaper rash

Table III

③ 目視判定結果	① 実施例					② 比較例
	1	2	3	4	5	1
著効 ④	6	10	8	9	7	0
有効 ⑤	2	0	1	1	2	1
やや有効 ⑥	2	0	1	0	1	1
無効 ⑦	0	0	0	0	0	8
悪化 ⑧	0	0	0	0	0	0

- Key: 1 Application example
 2 Comparative example
 3 Naked eye examination result
 4 Markedly effective
 5 Effective
 6 Slightly effective
 7 Ineffective
 8 Worsening

In the table, the number of subjects showing respective results of examination are represented.

As apparent from the results shown in Table III, the effectiveness of examples of the composition of this invention (Application Examples 1-5) was found to be apparently superior to that of the control composition (Comparative Example 1). Furthermore, the cleaning power of the composition of this invention was found to be excellent.

Application Example 6

Cleaning and wiping agent	wt%
(1) Purified water	remainder
(2) Glycerol	4.0
(3) Dipropylene glycol	7.0
(4) Ethanol	25.0
(5) Polyoxyalkylene-modified organopolysiloxane (polyoxyethylene group: 60 wt%, mean molecular weight of 10,000)	3.0
(6) Perfume	Suitable amount
(7) Tosyllysine	1.5

Application Example 7

Cleaning wet tissue stock solution

	wt%
(1) Purified water	remainder
(2) Ethanol	50.0
(3) p-Aminobenzamidine	0.08

(4) Perfume

Suitable amount

Application Example 8

Cleaning oil

	wt%
(1) Liquid paraffin	Remainder
(2) Neopentyl glycol dicaprate	8.0
(3) Squalane	2.5
(4) Olive oil	2.0
(5) Tocopherol acetate	0.1
(6) Cyclohexylguanidine	0.7

The safety and cleaning effects of Application Examples 6-8 were found to be excellent.

